

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
20 October 2005 (20.10.2005)

PCT

(10) International Publication Number  
**WO 2005/098448 A3**

- (51) International Patent Classification<sup>7</sup>: **C12Q 1/68**,  
C07H 21/02, 21/04
- (21) International Application Number:  
PCT/US2005/009874
- (22) International Filing Date: 24 March 2005 (24.03.2005)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/556,645 26 March 2004 (26.03.2004) US
- (71) Applicant (for all designated States except US): **MERCK & CO., INC.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **HARDWICK, James** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **DAI, Hongyue** [CN/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **LAMB, John, R.** [GB/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **SEPP-LORENZINO, Laura** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **SEVERINO, Michael, E.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **ZHANG, Chunsheng** [CN/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).
- (74) Common Representative: **MERCK & CO., INC.**; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report:  
29 December 2005
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD AND BIOMARKERS FOR DETECTING TUMOR ENDOTHELIAL CELL PROLIFERATION

(57) Abstract: Methods, biomarkers and expression signatures are disclosed for assessing the proliferative rate of vascular endothelial cells. More specifically, the invention provides a set of genes which can be used as biomarkers and gene signatures for evaluating the pharmacodynamic effects of cancer therapies designed to regulate the proliferation of endothelial cells in tumor vasculature. In one aspect the invention provides a method of evaluating the efficacy of a compounds designed to inhibit kinase receptor activity, such as a mammalian KDR receptor activity.



WO 2005/098448 A3